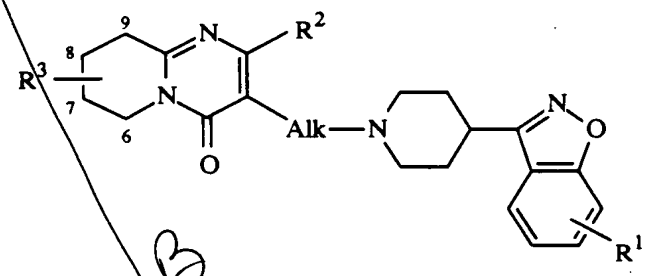
Claims

1. A compound having the formula



(I),

a pharmaceutically acceptable acid addition salt thereof, or a stereochemically isomeric form thereof, wherein

Alk is C_{1-4}alkanediyl;

R^1 is hydrogen, C_{1-4}alkyl or halo;

R^2 is C_{1-4}alkyl;

R^3 is hydroxy or R^4-C(=O)O-; and

R^4 is C_{1-19}alkyl.

2. A compound according to claim 1 wherein R^3 is substituted on the 9 position of the 6,7,8,9-tetrahydro-2-C_{1-4}alkyl-4H-pyrido[1,2-a]pyrimidin-4-one moiety.

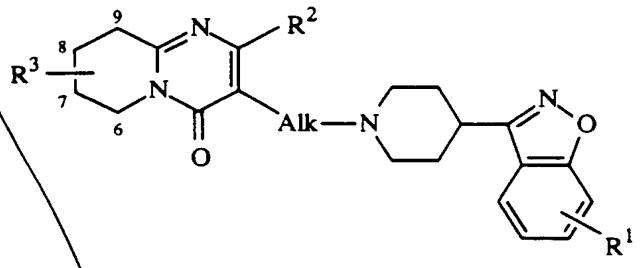
3. A compound according to claim 2 wherein Alk is ethanediyl, R^1 is halo and R^2 is methyl.

4. A compound according to claim 3 wherein R^1 is 6-fluoro.

5. A compound according to any of claims 1 to 4 wherein R^4 is heptyl, nonyl, undecyl or tridecyl.

6. A compound according to claim 1 wherein the compound is selected from 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, a pharmaceutically acceptable acid addition salt thereof, or an enantiomeric form thereof.

7. An antipsychotic composition comprising an inert carrier and as active ingredient an antipsychotic effective amount of a compound having the formula



(I),

a pharmaceutically acceptable acid addition salt thereof, or a stereochemically isomeric form thereof, wherein

Alk is C_{1-4}alkanediyl;

R^1 is hydrogen, C_{1-4}alkyl or halo;

R^2 is C_{1-4}alkyl;

R^3 is hydroxy or R^4-C(=O)O-; and

R^4 is C_{1-19}alkyl.

8. A composition according to claim 7 wherein R^3 is substituted on the 9 position of the 6,7,8,9-tetrahydro-2-C_{1-4}alkyl-4H-pyrido[1,2-a]pyrimidin-4-one moiety.

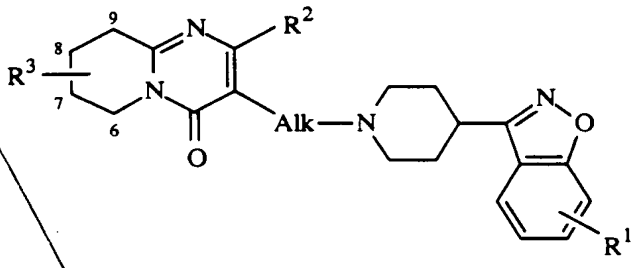
9. A composition according to claim 8 wherein Alk is ethanediyl, R^1 is halo and R^2 is methyl.

10. A composition according to claim 9 wherein R^1 is 6-fluoro.

11. A composition according to any of claims 7 to 10 wherein R^4 is heptyl, nonyl, undecyl or tridecyl.

12. A composition according to claim 7 wherein the compound is selected from 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, a pharmaceutically acceptable acid addition salt thereof, or an enantiomeric form thereof.

13. A method of treating warm-blooded animals suffering from psychotic diseases, which method comprises the administration to said warm-blooded animals of an antipsychotic effective amount of a chemical compound having the formula



(I),

a pharmaceutically acceptable acid addition salt thereof, or a stereochemically isomeric form thereof, wherein

Alk is C_{1-4}alkanediyl;

R^1 is hydrogen, C_{1-4}alkyl or halo;

R^2 is C_{1-4}alkyl;

R^3 is hydroxy or R^4-C(=O)O-; and

R^4 is C_{1-19}alkyl.

14. A method according to claim 13 wherein R^3 is substituted on the 9 position of the 6,7,8,9-tetrahydro-2-C_{1-4}alkyl-4H-pyrido[1,2-a]pyrimidin-4-one moiety.

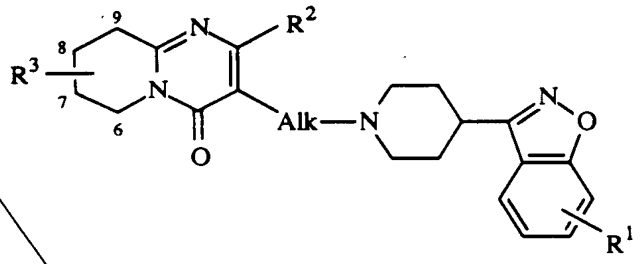
15. A method according to claim 14 wherein Alk is ethanediyl, R^1 is halo and R^2 is methyl.

16. A method according to claim 15 wherein R^1 is 6-fluoro.

17. A method according to any of claims 13 to 16 wherein R^4 is heptyl, nonyl, undecyl or tridecyl.

18. A method according to claim 13 wherein the compound is selected from 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one, a pharmaceutically acceptable acid addition salt thereof, or an enantiomeric form thereof.

19. A process for preparing a compound having the formula



(I),

a pharmaceutically acceptable acid addition salt thereof, or a stereochemically isomeric form thereof, wherein

Alk is C_{1-4}alkanediyl;

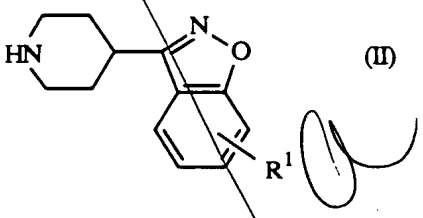
R^1 is hydrogen, C_{1-4}alkyl or halo;

R^2 is C_{1-4}alkyl;

R^3 is hydroxy or R^4-C(=O)O-; and

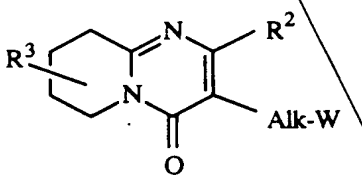
R^4 is C_{1-19}alkyl; characterized by

a) N-alkylating a 3-piperidinyl-1,2-benzisoxazole of formula



(II)

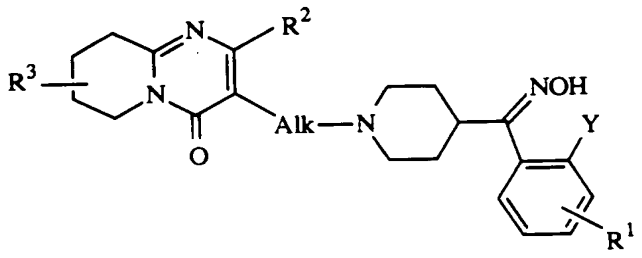
wherein R^1 is as defined under formula (I) with an alkylating reagent of formula



(III)

wherein R^2, R^3 and Alk are as defined under formula (I) and W represents a leaving group in a reaction-inert solvent at an elevated temperature;

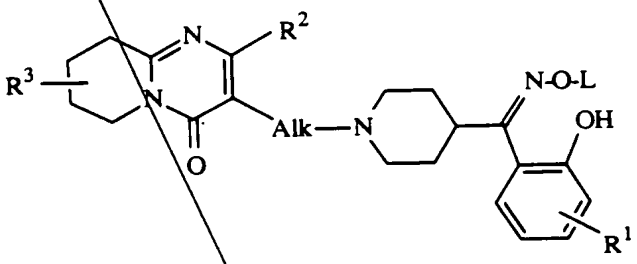
b) cyclizing an oxime of formula



(IV)

wherein R^1, R^2, R^3 and Alk are as defined under formula (I) and Y is a reactive leaving group in a reaction-inert solvent at an elevated temperature and in the presence of a base;

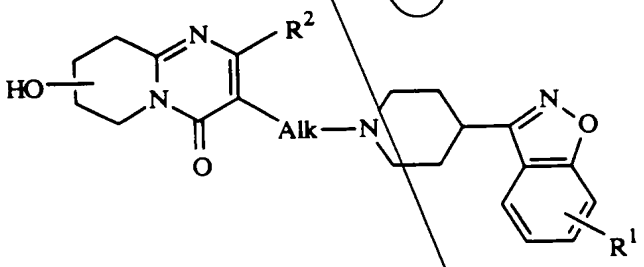
c) cyclizing an activated oxime derivative



(V)

wherein R^1, R^2, R^3 and Alk are as defined under formula (I) and L is an acid residue in a reaction-inert solvent at an elevated temperature and in the presence of a base;

d) O-acylating a compound of formula



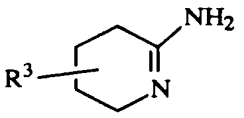
(I-a)

wherein R^1, R^2 and Alk are as defined under formula (I) with a carboxylic acid of formula

R^4-COOH (VI)

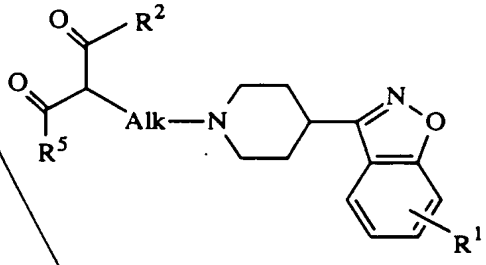
or a reactive functional derivative thereof, wherein R^4 is as defined under formula (I) in a reaction-inert solvent;

e) cyclizing an amidine of formula



(VII)

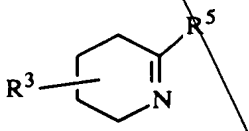
wherein R^3 is as defined under formula (I) with a β-dicarbonyl intermediate of formula



(VIII)

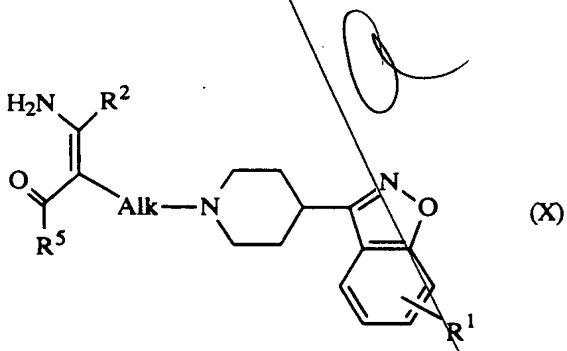
wherein R^1, R^2 and Alk are as defined under formula (I) and R^5 is a leaving group in a reaction-inert solvent at an elevated temperature;

f) cyclizing a reagent of formula



(IX)

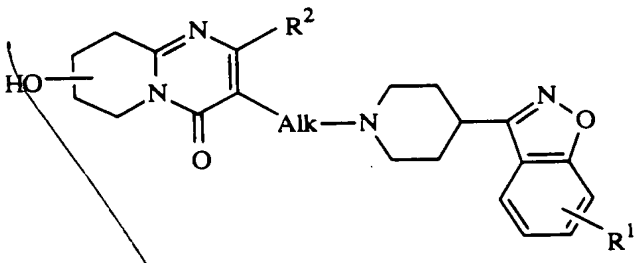
wherein R^3 is as defined under formula (I) and R^5 is a leaving group with an enamine of formula



(X)

wherein R^1, R^2 and Alk are as defined under formula (I) and R^5 is a leaving group, in a reaction-inert solvent at an elevated temperature; or

g) preparing the enantiomeric forms of the compounds of formula



(I-a)

wherein R^1, R^2 and Alk are as defined under formula (I), by converting the racemic mixtures of the compounds of formula (I-a) with a resolving agent to a mixture of diastereomeric salts or compounds, physically separating said mixture of diastereomeric salts or compounds and converting said separated diastereomeric salts or compounds into the corresponding enantiomeric forms of the compounds of formula (I-a);

and if desired, converting the compounds of formula (I) into a therapeutically active non-toxic acid addition salt form by treatment with an acid; or conversely, converting the acid salt into the free base with alkali;